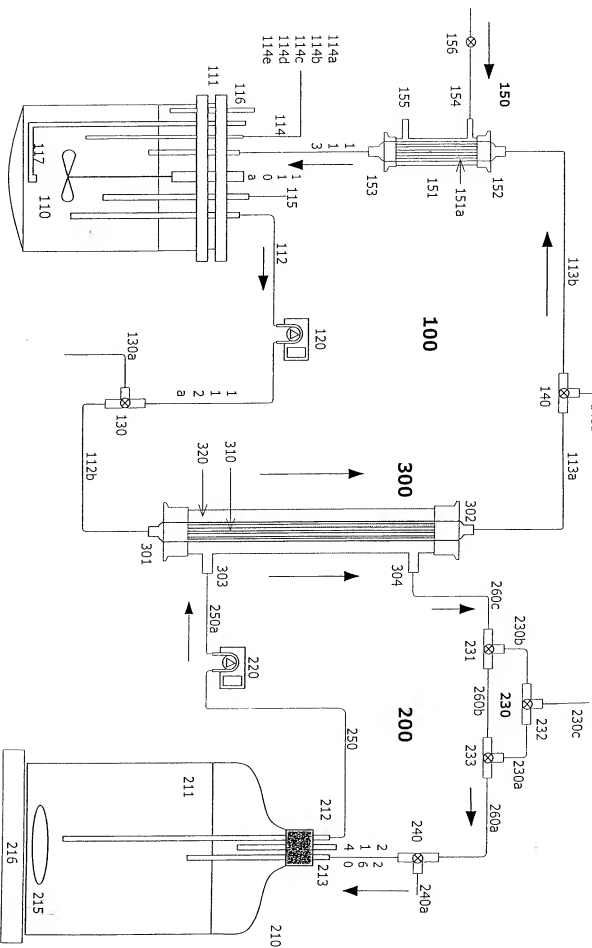


**Figure 1**

REPLACEMENT SHEET



Bioreactor

Media Reservoir

FIGURE 5 Growth of Insect Cells in a High-Density Dialysis Bioreactor with In-Line Oxygen Sparging.

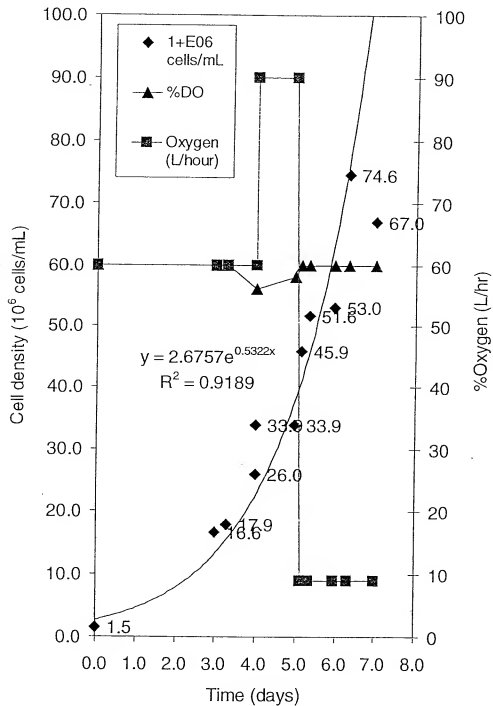


FIGURE 6      Yields of AcNPV Polyhedrin Protein in Standard and High-Density Cultures.

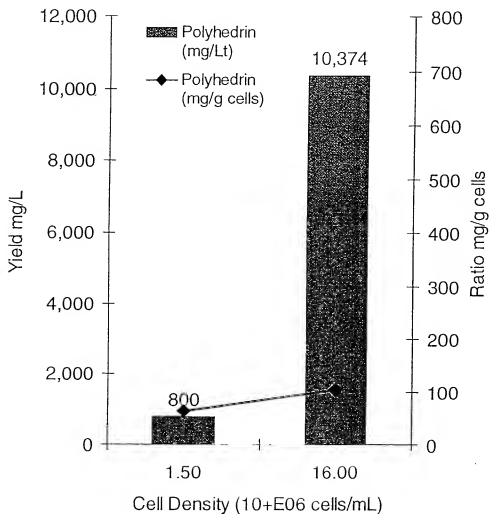
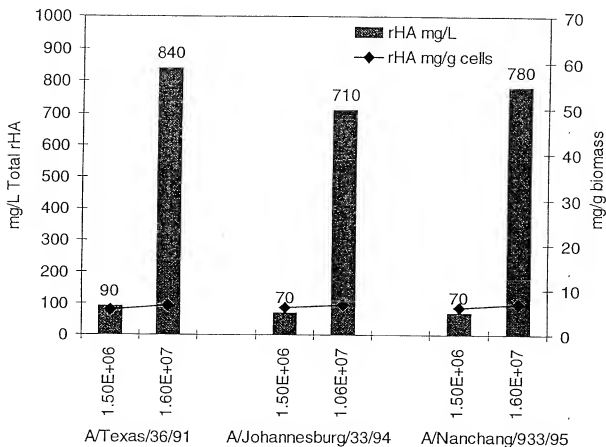
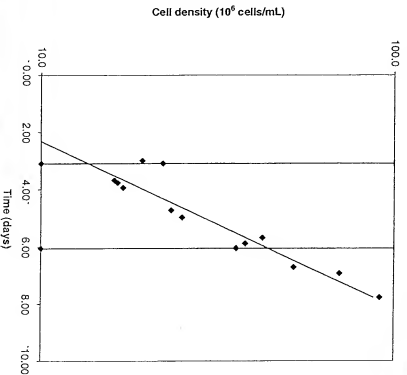


FIGURE 7 Yields of Recombinant Hemagglutinin from three Strains of Viral Influenza in Standard and High-Density Cultures.



| Time | Time (days) | Cell density (1E5 cells/mL) | Culture Vol (L) | Oxygen (L/hour) | Disolved air saturation (%) | Cell biomass (g/L) | Auxiliar Reserv. (L) |
|------|-------------|-----------------------------|-----------------|-----------------|-----------------------------|--------------------|----------------------|
| 8    | 4:00 PM     | 3.0                         | 1               | 6               | 60                          | 10                 | 10                   |
| 11   | 4:00 PM     | 19.4                        | 1               | 6               | 60                          |                    |                      |
| 11   | 6:20 PM     | 22.2                        | 1               | 6               | 60                          |                    |                      |
| 12   | 8:30 AM     | 3.69                        | 16.2            | 1               | 60                          |                    |                      |
| 12   | 10:30 AM    | 3.77                        | 16.5            | 1               | 60                          |                    |                      |
| 12   | 2:30 PM     | 3.94                        | 17.1            | 1               | 60                          |                    |                      |
| 13   | 9:20 AM     | 4.72                        | 23.4            | 1               | 60                          |                    |                      |
| 13   | 3:30 PM     | 4.98                        | 25.1            | 1               | 60                          |                    |                      |
| 14   | 8:30 AM     | 5.69                        | 42.4            | 1               | 60                          |                    |                      |
| 14   | 1:10 PM     | 5.88                        | 37.9            | 1               | 60                          |                    |                      |
| 14   | 5:00 PM     | 6.04                        | 35.7            | 1               | 60                          |                    |                      |
| 15   | 9:00 AM     | 6.71                        | 52.2            | 1               | 1.2                         | 60                 |                      |
| 15   | 2:10 PM     | 6.92                        | 70.2            | 1               | 1.2                         | 60                 |                      |
| 16   | 10:30 AM    | 7.77                        | 91.0            | 1               | 1.2                         | 60                 |                      |



Influence of Media Regeneration by Diffiltration on SF+ Cell Growth

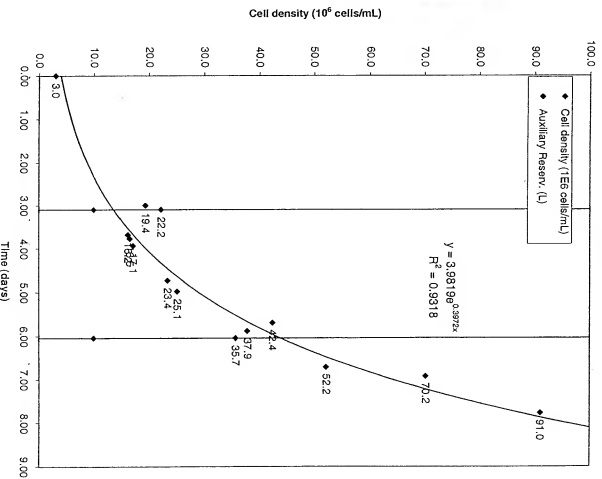


FIGURE 8

**Figure 9****HD Bioreactor Diagram Legend****100 Cell Culturing Loop**

|     |     |   |
|-----|-----|---|
| 110 |     | Stirred-tank Bioreactor                       |
|     | 111 | Bioreactor headplate                          |
|     | 112 | Cell take-up & cell take-up lines (112a – b)  |
|     | 113 | Cell return & cell return lines (113a – b)    |
|     | 114 | Probe ports: multiple (114a – 114e)           |
|     | 115 | Sampling port                                 |
|     | 116 | Vent tube                                     |
|     | 117 | Sparging tube                                 |
| 120 |     | Pump  |
| 130 |     | Three-way valve & three-way valve line (130a) |
| 140 |     | Three-way valve & three-way valve line (140a) |
| 150 |     | Oxygenation Loop                              |
|     | 151 | Oxygenator & oxygenator Lumen (151a)          |
|     | 152 | Lumen input                                   |
|     | 153 | Lumen outflow                                 |
|     | 154 | Gas input                                     |
|     | 155 | Gas output                                    |
|     | 156 | Solenoid                                      |

**200 Medium Replenishment Loop**

|     |     |   |
|-----|-----|---|
| 210 |     | Media reservoir   |
|     | 211 | Media container   |
|     | 212 | Media take-up   |
|     | 213 | Media return  |
|     | 214 | Vent tube   |
|     | 215 | Magnetic stir bar   |
|     | 216 | Variable speed magnetic motor                                       |
| 220 |     | Pump  |
| 230 |     | "Extraction" loop and "extraction" loop lines (230a – c)            |
|     | 231 | Three-way valve: pass-through or bypass in-line analysis            |
|     | 232 | Three-way valve: collection or sampling                             |
|     | 233 | Three-way valve: pass through or return                             |
| 240 |     | Three-way valve – sampling & three-way valve – sampling line (240a) |
| 250 |     | Media take-up lines (250 & 250a)                                    |
| 260 |     | Media return lines (260 & 260a – c)                                 |

**300 Hollow Fiber Dialysis Device**

|     |     |                       |
|-----|-----|-----------------------|
|     | 301 | Lumen input           |
|     | 302 | Lumen outflow         |
|     | 303 | Extra-lumenal input   |
|     | 304 | Extra-lumenal outflow |
| 310 |     | Lumen space           |
| 320 |     | Extra-lumen space     |

| Days | Cell/ml $\times 10^6$        |                       |
|------|------------------------------|-----------------------|
|      | High density bioreactor (2L) | Control flask (0.1 L) |
| 0    | 0.9                          | 0.9                   |
| 1    | 1.3                          | 1.8                   |
| 2    | 2.4                          | 3.0                   |
| 3    | 4.3                          | 4.6                   |
| 4    | 7.8                          | 4.1                   |
| 5    | 13.6                         |                       |

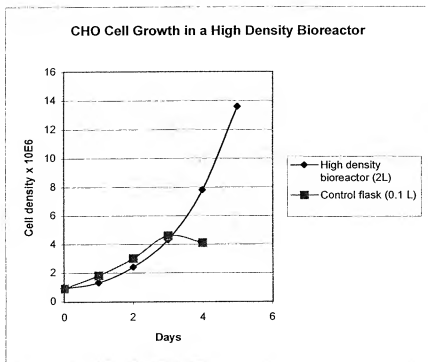


FIGURE 11